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09/701,747	01/29/2001	John N. Wood	620-123	8145

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EXAMINER
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ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/701,747	Wood et al
Examiner	**Art Unit**
Nirmal S. Basi	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 20, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above, claim(s) *28-32, 36, 43, and 45* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-27, 33-35, 37-42, and 44* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Response filed 8/20/02 (paper number 11) has been entered.

2.. Applicant's election with traverse of Group 1 (Claims 1-19 , 21-27 and 38-41), in Paper No. 11, is acknowledged. The traversal is on the ground(s) that the requirement of unity of invention referred to in rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. Applicant argues there is a relationship of a technical feature involving Groups I-IX. Applicants arguments have been fully considered and found persuasive in part. Claims 20, 33-35, 37 and 42 are rejoined because they relate to a single inventive concept and constitute the product, first method of making the product and first method of use of the product. Claims 1-27 , 33-35, 37-42 will be examined.

3. **Objections**

Applicants are required to use the heading "Brief Description of the Drawings" to describe the drawings. See MPEP 608.01(f). On page 27, Applicant has written “Figures”.

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

5. The drawings objected to because each Figure must described separately in the Brief Description of the Drawings as Figure 1A, 2B, 3C and 4D

Appropriate correction is required.

6. ***Sequence Rules Compliance***

This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences in Figures 1A-D must be identified by their corresponding SEQ ID NO:. Compliance with sequence rules is required.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1-15, 37-40 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-15, 37-40 recite a nucleic acid, polypeptide or protein but do not recite that they are isolated or purified. The claims as currently recited encompass these naturally-occurring compounds. Therefore, the compounds as claimed are a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It is suggested that the claims be amended to recite "an isolated and purified" to overcome this rejection.

Claim 1-13, 15, 33 38 and 44 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255

F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). Amending the claim to recite "a process or a method" will obviate this rejection.

Claim Rejection, 35 U.S.C. 112

8. Claims 1-27 , 33-35, 37-42 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it is not clear what is implied by acid sensitive so as to allow the metes and bounds of the claim to be determined. For example acid sensitive can mean sensitive to acids so that the cation channel protein may be susceptible to denaturation by acids or the currents mediated by cation channel may be sensitive to changes in acidic pH. Further, it is not clear how the protein is sensitive to acid and what parameter is used to determine sensitivity.

Claims 2, 7, 16 are indefinite because it is not clear what activity is contained by ion channel so as to allow the metes and bounds of the claim to be determined.

Claim 4 is indefinite because it is not clear what is rapid cation so as to allow the metes and bounds of the claim to be determined. The term "rapid" in claim 4 is a relative term which renders the claim indefinite. The term "rapid" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. When is a current rapid as compared to not

rapid so as to allow the metes and bounds of the claim to be determined. Further it is not clear what is a sustained cation current and when it is considered rapid and sustained.

Claim 8 is indefinite because the complete hybridization conditions are not specified, ie, no wash conditions are specified. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed **including wash conditions**. Since the hybridization and wash conditions dictate which DNA sequences remain specifically bound to a particular nucleic acid the metes and bounds of the claims cannot be determined without the disclosure of said conditions.

Claim 11 is indefinite because for the use of the term either. Either, as interpreted by Examiner, means one or the other. The term "either" can apply to more than two items i.e. to 30 or 50 or 100 bases or degeneratively equivalent. Similarly claim 12 is indefinite for use of either.

The term "highly conserved" in claim 13 is a relative terms which renders the claim indefinite. The term "highly conserved" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Further in claims 13 and 14 it is not clear which sequence of proteins are considered DRASIC, α-ASIC and β-ASIC so as to allow the metes and bounds of the claim to be determined and allow a meaningful comparison of said proteins. It is suggested DRASIC, α-ASIC and β-ASIC be identified by SEQ ID NO:.

Claim 7 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s),

or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 7 recites "at least 80% sequence identity with the full length sequence as shown in SEQ ID NO:2" when referring to the nucleic acid of claim 5, claim 5 depends on claim 1 which refers to the protein of SEQ ID NO:2. Therefore claim 7 is not further limiting.

Claim 8 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 7 recites a nucleic acid capable of hybridizing under high stringency conditions when referring to the nucleic acid of claim 7. The number of species capable of hybridizing to said nucleic acid are greater in number than those contained in the base claims and therefore not further limiting.

Claims 9, 16 and 40 recite "allelic variant, it is unclear what is an "allelic variant". The term "variant" carries no weight in terms of structure and function and encompasses an unlimited number of alterations and reads on unrelated molecules. Further since no allele is disclosed it is not clear what would be considered an allelic variant so as to allow the metes and bounds of the claim to be determined.

Claim 16 is indefinite because the method steps do not achieve the goal of identifying and/or cloning a nucleic acid which encodes a SPASIC variant as stated in the preamble. An acceptable method claim must contain three sections: 1) a preamble, 2) method steps that clearly define what is to be done in each step, and 3) a conclusion that what was stated in the preamble was

achieved (the method does not contain specific assay steps and a statement how and when the goal of the claim is achieved). The claim does not set forth any steps involved in the method and a statement how and when the goal of the claim is achieved. Further, claim 16 is indefinite because it is not clear if the claim is drawn to a method of identification or a method of cloning or both. It is not clear what sequence is referred to by the phrase "said sequences" . Claim 16 recites the limitation "said sequences" in line 7. Also, it is not clear how the first nucleic acid molecule is employed and what is meant by employed so as to allow the metes and bounds of the claim to be determined. The use of the word first nucleic acid infers a second nucleic acid. It is not clear what is the second nucleic acid.

Claim 17 is indefinite because the conditions for complete hybridization. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed including wash conditions. Since the hybridization and wash conditions dictate which DNA sequences remain specifically bound to a particular nucleic acid the metes and bounds of the claims cannot be determined without the disclosure of said conditions.

Claim 18 is indefinite because it is not clear when molecule primer is considered suitable for PCR as compared to when it is not considered suitable for PCR. The use of the word pair of nucleic acid molecule primers infers a second nucleic acid molecule. It is not clear what is the second nucleic acid. It is not clear what determines the presence or absence of the PCR product and that

what was stated in the preamble was achieved (the method does not contain specific assay steps and a statement how and when the goal of the claim is achieved)

Claims 19 and 41 is indefinite because it is not clear what is implied by the term "derived from" so as to allow the metes and bounds of the claims to be determined. The ambiguity in the claim lies in the meaning of the word "derived". Derived can mean to obtain from (purified from) or created by chemical conversion from.

Claims 20 and 42 recites the limitation "derivative" in claim 7 and 8, respectively. There is insufficient antecedent basis for this limitation in the base claims.

Claims 20 and 42 recite "derivative", it is unclear what is a "derivative". The term "derivative" carries no weight in terms of structure and function and encompasses an unlimited number of alterations and reads on unrelated molecules. Therefore the metes and bounds of the claim cannot be determined. Further it is not clear what is implied by modifying. Modify means to change. It is not clear how and what is changed in the nucleic acid.

Claim 33 is indefinite because the method steps do not achieve the goal of identifying a substance having ion-channel modulating activity as stated in the preamble. An acceptable method claim must contain three sections: 1) a preamble, 2) method steps that clearly define what is to be done in each step, and 3) a conclusion that what was stated in the preamble was achieved (the method does not contain specific assay steps and a statement how and when the goal of the claim is achieved). The claim does not set forth any steps involved in the method and a statement how and

when the goal of the claim is achieved. Further, claim 16 is indefinite because it is not clear what activity is modulated or how the protein is used.

Claim 34 is indefinite because it is not clear what protein is exposed, what and how the electrophysiological response of the cell or membrane is measured and related to the interaction of the substance and the protein, and how and when the goal of the claim is achieved.

Claim 35 is indefinite because it is not clear when the method identifies the substances as potential analgesics, neuromodulatory agents, anti-inflammatory agents, agents that regulate neurotransmitter release or neuronal excitability as compared to those agents that are not potential analgesics, neuromodulatory agents, anti-inflammatory agents, agents that regulate neurotransmitter release or neuronal excitability.

Claim 38 is indefinite because it is not clear what is inferred to by "containing the same" so as to allow the metes and bounds of the claim to be determined.

Claim 39 is indefinite because it is not clear what is considered a pain response so as to allow the metes and bounds of the claim to be determined.

Claim 42 is indefinite because the method steps do not achieve the goal of producing a derivative nucleic acid molecule as stated in the preamble. An acceptable method claim must contain three sections: 1) a preamble, 2) method steps that clearly define what is to be done in each step, and 3) a conclusion that what was stated in the preamble was achieved (the method does not contain specific assay steps and a statement how and when the goal of the claim is achieved). The

claim does not set forth any steps involved in the method and a statement how and when the goal of the claim is achieved.

Claim 44 is indefinite because the method steps do not achieve the goal of identifying a substance having ion-channel modulating activity as stated in the preamble. An acceptable method claim must contain three sections: 1) a preamble, 2) method steps that clearly define what is to be done in each step, and 3) a conclusion that what was stated in the preamble was achieved (the method does not contain specific assay steps and a statement how and when the goal of the claim is achieved). The claim does not set forth any steps involved in the method and a statement how and when the goal of the claim is achieved. Further, claim 44 is indefinite because it is not clear what activity is modulated or how the cell is used.

Claim 26 is an improper Markush group. Claim 26 contains both a genus and species of cells.

Claims 38 and 39 are rejected because they do not further limit the base claim. The claimed uses do not provide a further structural or functional limitation on the claim.

Claims 3, 5, 7, 10, 15, 21-25, 27 and 37 are rejected for depending upon an indefinite base (or intermediate) claim and fail to resolve the issues raised above.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-27 , 33-35, 37-42 and 44 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to nucleic acid (SEQ ID NO:1) encoding the cation channel SPASIC polypeptide (SEQ ID NO:2), variants thereof (including allelic variants), probes and primers comprising fragments of the nucleic acid of SEQ ID NO:1, method of identifying/cloning nucleic acid encoding the variant SPASIC protein (at least 80% identical)using PCR and hybridization, producing derivatives of SPASIC protein and nucleic acid encoding SPASIC protein, vectors comprising SPASIC nucleic acid, cell containing said vector, method for identifying substance with ion-channel modulating activity using said protein and said cell.

Further, claims 38 and 39 infer the use of claimed nucleic acid in inhibiting pain response/altering neurotransmittrer release, gene therapy and preparation of a medicament.

A “specific utility” is a utility that is specific to the subject matter claimed, as opposed to a “general utility” that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention.

Applicant has asserted utilities for the specifically claimed invention of claims 1-27 , 33-35, 37-42 and 44. The utilities disclosed in the specification are based on methods using SPASIC protein (H+ gated cation channel from rat sensory neuron) as a target for screening for agents that regulate neurotransmitter release or neuronal excitability, treatment in SPASIC-mediated and related disorders and to identify agonists and antagonists for diagnosis and treatment.

The specification discloses (:

a) SPASIC has 43% identity with ASIC (amiloride-sensitive Na+ channel (page 2).

b) SPASIC has unique properties, it exhibits both a rapid, and then a sustained cation current in response to low pH. The specification specifically states "No H+-gated channel having these properties has been characterized" (page 2).

c) Because of the expression of SPASIC in sensory neurons and the importance of proton-gated channels in pain and inflammation, this new channel is an angelegic drug target (page 3).

In light of the specification the skilled artisan can conclude that the nucleic acid of SEQ ID NO:1 encodes the SPASIC H+gated cation channel of SEQ ID NO:2 (Examiners conclusion based on Figure 2). It is presumed that Figure 2 shows the functional SPASIC H+gated cation channel of

SEQ ID NO:2 contained in a cell. There is no disclosure that SPASIC has properties identical to ASIC or that it is even an amiloride-sensitive Na+ channel. Since the specification discloses no H+-gated channel having the properties of SPASIC has been characterized it follows that functional properties of SPASIC cannot be predicted by comparison to known ion channels with different ion gating properties. Further because SPASIC is expressed in sensory neurons it does not necessarily follow that it is important in the management of pain and inflammation or that it is an angelegic drug target. Many proteins are found in sensory neurons, all are not important in the management of pain and inflammation, or are targets for angelegic drugs.

No disclosure is provided within the instant specification on what specific function a putative SPASIC protein possesses, ligands that activate, nor are any disease states disclosed that are directly related to SPASIC dysfunction. There is no data in the specification or prior art that SPASIC can be used management of pain and inflammation or that it is an angelegic drug target.

The specification discloses that the claimed polynucleotides and proteins are useful as tools for drug discovery, screening assays and the diagnosis of disease. For a utility to be "well-established" it must be specific, substantial and credible. All nucleic acids and genes and their encoded polypeptides may in some combination be useful in drug discovery, screening assays and the diagnosis of disease. However, the particulars of testing with SEQ ID NO:2 or SEQ ID NO:1 are not disclosed in the instant specification. Neither the specific disease states, screening assays or ligands that bind to the SPASIC of instant invention are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of

proteins or DNA, but is only potential with respect to SEQ ID NO:2 SEQ ID NO:1. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polynucleotide in an array for screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Applicants' individual polynucleotide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polynucleotide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this nucleic acid could be put.

With regard to diagnosis of disease, in order for a polynucleotide or protein to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polynucleotide and a disease or disorder. The presence of a polynucleotide in neuronal tissue is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed cDNA or protein and the disease. If a molecule is to be used as a surrogate

for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. over expression). Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

The specification fails to disclose sufficient properties of the protein and/or polynucleotide (SEQ ID NO:1 and 2) to support an inference of utility. The SPASIC protein belongs to the family ion channels in which the members have divergent functions. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such

as proteases, ligases and telomerases share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

Without some common biological activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. To argue that all the members can be used for screening/testing for drugs, and diagnosis of disease, is to argue a general, nonspecific utility that would apply to virtually every member of the family, contrary to the evidence. Further, any compound could be considered as a regulator or modulator of tissue in that any compound, if administered in the proper amount, will stimulate or inhibit tissue. For example, salt, ethanol, and water are all compounds which will kill cells if administered in a great enough amount, and which would stimulate cells from which these compounds had been withheld, therefore, they could be considered regulators or modulators of tissue. However, use of these compounds for the modulation of tissue would not be considered a specific and substantial utility unless there was some disclosure of, for example, a specific and particular combination of compound/composition and application of such in some particular environment of use.

Without knowing a biological significance of the claimed polypeptides or the polynucleotides or the polypeptide encoded thereby, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible "real world" manner based on the diversity of biological activities possessed by the ion channel. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

The present rejection under § 101 follows *Brenner v. Manson*, as set forth above. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. As Applicant recognizes, a rejection under § 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

Therefore, for reasons set forth above, the methods of use of SPASIC protein and nucleic acid of instant invention are also rejected for lack of utility.

12. Claims 1-27 , 33-35, 37-42 and 44 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the SPASIC nucleic acid/protein/vectors/cells/variants/methods of, further experimentation is necessary to attribute a utility to the claimed SPASIC nucleic acid/protein/vectors/cells/variants/methods.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Further, many of the polypeptides, encoded by the nucleic acids which hybridize to the polynucleotide of SEQ ID NO:1, unrelated to the SPASIC of instant invention. The specification does not disclose a utility for or how to use unrelated polypeptides. Furthermore, the nucleic acid hybridizing to the nucleic acid of SEQ ID NO:1, the "sense strand", would encode proteins which would be expected to be inactive. The wash conditions in the hybridization have not been provided.

Therefore the hybridization conditions recited in the claim do not constitute a meaningful structural limitation.

Pertaining to claims 8 and 37 the instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The only disclosed compound in both the instant case and in Ex parte Maizel was the full length, naturally occurring protein. The Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents would consist of proteins having amino acid substitutions wherein the substituted amino acids have similar hydrophobicity and charge characteristics such that the substitutions are "conservative" and do not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, a single disclosed sequence does not support claims to: (a)any nucleic acid hybridizing to same, given the lack of guidance regarding what sequences would hybridize specifically to SEQ ID NO: 2, and not other, related sequences, or (b) to polypeptide comprising an antigen-binding site of an antibody capable of specifically binding the protein of SEQ ID NO:1 or variants thereof. Further, many of the polypeptides encoded by the nucleic acids isolated by hybridization or binding to antibody will be unrelated to the protein of instant invention, being devoid of its characteristic structural and

functional features. Said unrelated polypeptides isolated by hybridization may be produced by frame shift in the coding sequence of the nucleotide, for example. Other polypeptides may be truncated, for example. Due to the large quantity of experimentation necessary to identify the polypeptides with the structural and functional features of instant invention, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said polypeptides, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:1 are also encompassed by the claim), and the breadth of the claim which fail to recite structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

Furthermore, the specification does not reasonably provide enablement for the scope of use of probes and primers comprising specific sequences of SEQ ID NO:1. Said probes and primers may not be specific for the polynucleotide of SEQ ID NO:2. The specification has not disclosed how to use said non-specific probes and primers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification discloses a polynucleotide of SEQ ID NO:1 encodes the SPASIC protein of SEQ ID NO:2. The specification does not teach how to make functional SPASIC variants or fragments of SPASIC protein which retain activity, nor does it show how to use inactive variants. There is no disclosure of the structure of the allelic variant (intron/exons) or that an allelic variant

even exists. Further pertaining to variants and functional derivatives/derivatives the prior art teaches that amino acid substitutions produce unpredictable results in a structurally related protein. Furthermore, neither the specification nor the prior art provide any guidance as to which amino acids could be altered to retain functionality, which domains are important for function, nor does the specification provide any guidance as to how the skilled artisan could use an inactive SPASIC derivatives. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation that an variants/derivatives could be used for any purpose.

Further, claims 38-39 claims are rejected based on the failure of the specification to enable one of skill in the art to make and/or use the nucleic acids in the preparation of a pharmaceutical composition/gene therapy. The specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the SPASIC protein as a drug or medication commensurate in scope with the claim without undue experimentation. Further there is no disclosure of the use of claimed nucleic acid in the complicated science of gene therapy. There is no disclosure that there is a disfunction that could be rectified by use of the nucleic acid of SEQ ID NO:1. Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (8 USPQ2d 1400 (CA FC 1988)). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented. The term medicament and gene therapy imply a treatment of a disease. It is unpredictable what diseases could

be effectively treated using claimed invention. Neither the specification nor the prior art provide sufficient guidance as to what specific diseases could be treated by administering a SPASIC nucleic acid or protein. Attempting to identify a disease treatable by such a composition would constitute undue experimentation. Therefore, the unpredictability to achieve all the afore mentioned goals and the lack of guidance provided in the specification, the disclosure fails to enable one of skill in the art how to make and/or use the nucleic acid in a medicament and gene therapy encompassed by the claims.

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. A review of *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) clearly points out the factors to be considered in determining whether a disclosure would require undue experimentation and include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors are considerations when determining the whether undue experimentation would be required to use the claimed invention. As is evidence in the discussions above, each of these factors has been carefully considered in the instant grounds of rejection, and it is considered that undue experimentation would be required by the skilled artisan to use the instant invention.

13. Claims 2-14, 1627 , 33-35, 37-42 and 44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acid (SEQ ID NO:1) encoding the cation channel SPASIC polypeptide (SEQ ID NO:2), variants thereof (including allelic variants), probes and primers comprising fragments of the nucleic acid of SEQ ID NO:1, method of identifying/cloning nucleic acid encoding the variant SPASIC protein (at least 80% identical)using PCR and hybridization, producing derivatives of SPASIC protein and nucleic acid encoding SPASIC protein, vectors comprising SPASIC nucleic acid, cell containing said vector, method for identifying substance with ion-channel modulating activity using said protein and said cell.

The claims, as written, encompass polypeptides which vary substantially in length and also in amino acid composition. The instant disclosure of a polynucleotide of SEQ ID NO:1 encoding the polypeptide of SEQ ID NO:2 does not adequately describe the scope of the use of the claimed genus of polypeptides, which encompasses a substantial variety of subgenera including full-length proteins/nucleic acids, chimeric proteins/nucleic acids, fusion proteins/nucleic acids, allelic variants, and variants. The variants (with no known or disclosed function) can be encoded by nucleic acids which hybridize to the polynucleotide of SEQ ID NO:1. The polypeptides, encoded by polynucleotides isolated by hybridization to the nucleic acid of SEQ ID NO:1, may be completely unrelated to the polypeptide of SEQ ID NO:1. Further, polypeptides, comprising fragments and variants of SEQ ID NO:2, may also, be completely unrelated to the polypeptide of SEQ ID NO:2. A description of a genus of polypeptides may be achieved by means of a recitation of a

representative number of polypeptides, defined by amino acid sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. **The common function of the claimed genus of polynucleotides, which is based upon a common property or critical technical feature of the genus claimed is not disclosed.** For example, what regions and fragments of the polynucleotide of SEQ ID NO:1 or polypeptide of SEQ ID NO:2 contain a definitive structural feature required for protein function? The specification proposes to discover other members of the genus by using screening assays and techniques involving probes, primers, hybridization. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed. No identifying characteristic or property of the instant polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because

the genus is highly variant, the disclosure of specific polypeptide and nucleotide sequences and the inability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed.

The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins/nucleic acids and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

Furthermore, the written description is not commensurate in scope with the claims drawn to allelic variants of the amino acid sequence shown in SEQ ID NO:2 or encoded by the cDNA contained in SEQ ID NO:1.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Examiner has interpreted alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome and differing from other alleles of that locus at one or more mutational sites. Thus, the structure of claimed allelic variants sequences are not defined. With the exception of SEQ ID NO:1, encoding the protein of SEQ ID NO:2, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides or polypeptide and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". However, no disclosure, beyond the mere

mention of allelic variants is made in the specification. This is insufficient to support the generic claims for reasons given above.

Therefore only the use of isolated polypeptide shown in SEQ ID NO:2 encoded by DNA molecule comprising a DNA sequence consisting of nucleotides of SEQ ID NO:1, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Claim 26 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

14. The deposit of biological material is considered by the Examiner to be necessary for the enablement of the current invention because the claims require availability of the deposit. The deposit of host cells COS, CHO and HEK 293 is not in full compliance with 37 CFR §§ 1.803-1.809 because the specification does not provide a repeatable method for obtaining ATCC deposit and it does not appear to be a readily available material. Applicant must provide evidence that host cells COS, CHO and HEK 293 listed in instant application will be available under the criteria (I)-(V) listed below. Although, the aforementioned cells if available today from ATCC, may not be available in the future. An enabled ATCC deposit would satisfy the requirements of 35 USC §112, first paragraph.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit

has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(I) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(II) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(III) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(IV) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(V) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
November 2, 2002

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